Clinical Prediction Model for in-Hospital Mortality in Sepsis Patients Complicated by ARDS

ABSTRACT

Background

Acute Respiratory Distress Syndrome (ARDS), characterized by widespread lung inflammation and impaired gas exchange, is a devastating complication frequently driven by sepsis. Sepsis is implicated in up to 75% of ARDS cases, and the co-occurrence significantly increases mortality risk compared to ARDS from other causes. While the progression from sepsis to ARDS can be rapid, identifying which patients face the highest risk of mortality is difficult. Existing clinical scoring systems lack the necessary specificity, highlighting an urgent need for predictive models tailored to the sepsis-ARDS population.

Methods

4,379 patients diagnosed with Sepsis-3 and ARDS were extracted from the MIMIC IV (v3.1) database using ICD codes. Features with a target variable (In-Hospital Mortality) were selected based on backward selections with advice from senior medical specialists. Data preprocessing steps were performed in a traditional way, and class imbalance issue was handled using SMOTE. Six machine learning models were incorporated and implemented using different kinds of hyper parameter tuning methods: Logistic Regression, Random Forest, XGBoost, LightGBM, SVM, and KNN. Models were evaluated using matrices (accuracy, sensitivity, specificity, ROC-AUC, 95% confidence interval with lower and upper bound). ROC-AUC scores were used primarily for choosing the best model. At the end, SHAP evaluation was performed for the best selected model to explore features with significant influence.

Results

We assessed the performance of several machine learning models for predicting in-hospital mortality in patients with sepsis complicated by ARDS, focusing on Random Forest, XGBoost, LightGBM, Support Vector Machine (SVM), Logistic Regression, and K-Nearest Neighbors (KNN). Among these, Random Forest demonstrated superior performance, with an accuracy of 82.88%, sensitivity of 60.00%, and specificity of 89.21%, achieving the highest ROC-AUC score of 0.8682. XGBoost followed closely with an accuracy of 83.56% and an AUC of 0.8660, yielding comparable results. Both SVM and Logistic Regression exhibited notable sensitivity values (0.7474 and 0.7368, respectively), suggesting their efficacy in identifying true positive cases. In contrast, KNN demonstrated the weakest performance across all evaluation metrics, particularly in terms of AUC (0.8387).

Conclusions

This study developed a predictive model for in-hospital mortality among sepsis patients with ARDS using the MIMIC-IV database. By integrating 21 clinically relevant features and applying advanced preprocessing and feature selection techniques, we achieved strong model performance, with Random Forest emerging as the top-performing algorithm (AUC = 0.868).

Feature importance and SHAP analysis further enhanced model interpretability. The results highlight the value of early risk stratification in critical care and support the use of data-driven tools to improve outcomes in high-risk patient populations. Future work will focus on external validation and real-world application to assess clinical impact.

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1. INTRODUCTION

1.1 Background

Acute Respiratory Distress Syndrome (ARDS) represents a critical clinical challenge in intensive care medicine, characterized by widespread inflammation in the lungs leading to impaired gas exchange and hypoxemia [1]. In patients with sepsis, a condition defined by a dysregulated host response to infection causing life-threatening organ dysfunction, ARDS develops as a devastating complication with shared underlying mechanisms of inflammation and endothelial dysfunction. The co-occurrence of these conditions creates a particularly high-risk scenario for patients.

Sepsis is recognized as the primary cause of ARDS, accounting for approximately 31% of all ARDS cases, with extreme hypoxia contributing to roughly 38.2% of mortality in intensive care units (ICUs). Recent international studies indicate that sepsis underlies approximately 75% of ARDS cases (59% from pneumonia and 16% from extrapulmonary sepsis), and the mortality rate for patients with severe ARDS ($PaO_2/FiO_2 < 100$) approaches 40%.

The epidemiological burden is substantial. According to multicenter studies, the overall 30-day attributable mortality of ARDS among critically ill patients with sepsis is approximately 11.9%, with increasing severity of ARDS correlating with higher mortality rates. Specifically, the 30-day attributable mortality rates for mild, moderate, and severe ARDS are estimated at 10.5%, 11.6%, and 18.1%, respectively, demonstrating the progressive impact of ARDS severity on patient outcomes [2].

This mortality risk is compounded by the rapid progression from sepsis to ARDS, which typically occurs within 12-48 hours after admission, leaving a narrow window for intervention. Despite advances in critical care medicine, our ability to predict which sepsis patients will develop ARDS, and subsequently which of those will experience poor outcomes, remains limited.

1.2. Problem Statement

The combination of sepsis and ARDS creates a clinical scenario with significantly elevated morbidity and mortality compared to either condition alone. Notably, patients with sepsis-induced ARDS demonstrate higher mortality rates than those with ARDS from other causes, suggesting unique sepsis-activated molecular pathways that result in particularly severe manifestations of ARDS.

Current clinical scoring systems, while valuable for general ICU risk stratification, lack specificity for the sepsis-ARDS population. Recent studies utilizing machine learning approaches have identified key factors associated with sepsis-ARDS mortality, including age, body mass index (BMI), biochemical markers (such as blood urea nitrogen, lactate, creatinine), and comorbid conditions, achieving accuracies between 71.8% and 81.4% in predicting mortality outcomes [2].

However, there remains a critical need for a comprehensive, validated predictive model that can accurately estimate in-hospital mortality specifically for patients with sepsis complicated by ARDS. Such a model would serve multiple purposes:

1. Enabling early identification of high-risk patients who may benefit from more aggressive interventions or experimental therapies
2. Facilitating more informed discussions with patients and families regarding prognosis and goals of care
3. Providing a standardized tool for risk stratification in clinical research and quality improvement initiatives
4. Supporting resource allocation decisions in healthcare systems, particularly during periods of high demand

The development of a robust predictive model requires integration of multiple clinical variables, including physiological parameters, laboratory values, comorbidities, and treatment modalities, all explicitly calibrated to the unique pathophysiology of sepsis-ARDS. This paper aims to address this gap by developing and validating such a model to enhance clinical decision-making and ultimately improve outcomes for this vulnerable patient population [3].

2. METHODOLOGY

2.1. Database Description

This study utilized data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, version 3.1. MIMIC-IV is a large, single-center, freely accessible database developed through a collaboration between Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts, and the Massachusetts Institute of Technology (MIT). The database contains comprehensive, de-identified clinical data from patients admitted to various intensive care units (ICUs) and emergency departments at BIDMC between 2008 and 2022 [5]. The use of the MIMIC-IV database was approved by the Institutional Review Boards of BIDMC and MIT, with a waiver of informed consent due to the retrospective nature of the study and the de-identification of all patient data in accordance with the Health Insurance Portability and Accountability Act (HIPAA) Safe Harbor provision [7].

MIMIC-IV adopts a modular approach to data organization, which facilitates the integration of disparate data sources. The database contains detailed clinical information, including patient demographics, vital sign measurements, laboratory test results, medication administration records, procedures, diagnoses using International Classification of Diseases (ICD) codes, clinical notes, imaging reports, and mortality data (both in-hospital and up to one year post-discharge) [3]. Physiological data are recorded at high temporal resolution, with vital signs typically documented hourly and laboratory data available as ordered throughout the patient's stay.

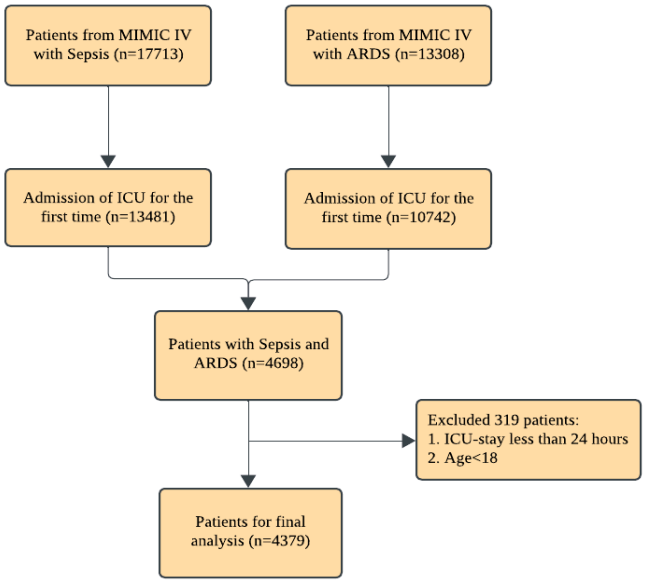
For our study on sepsis and Acute Respiratory Distress Syndrome (ARDS), we leveraged multiple components of the MIMIC-IV database to identify patients meeting Sepsis-3 criteria, which defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection [4]. This was operationalized as patients with suspected or confirmed infection (identified through culture data and antibiotic administration) plus an acute increase in Sequential Organ Failure Assessment (SOFA) score of $\geq$2 points. ARDS was identified using the Berlin definition, which requires: (1) onset within one week of a known clinical insult or new/worsening respiratory symptoms; (2) bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules; (3) respiratory failure not fully explained by cardiac failure or fluid overload; and (4) decreased oxygenation with a PaO_2/FiO_2 ratio $\leq$ 300 mmHg with a minimum PEEP of 5 cmH_2O.

The use of MIMIC-IV for this study provides several advantages, including its large sample size, granular clinical data with precise timestamps, and the ability to track patient outcomes throughout their hospitalization. The database's structure allows for the extraction of features

relevant to sepsis and ARDS prediction, including physiological parameters, laboratory values, and timing of interventions, which are critical for developing accurate predictive models for in-hospital mortality.

2.2. Patient Inclusion Criteria

Data from the MIMIC IV (v3.1) was selected based on inclusion and exclusion criteria. Adult patients diagnosed with sepsis-3 and ARDS who met the criteria were included in this research. As shown in the following figure, the inclusion criteria were applied: (1) patients diagnosed with both sepsis-3 and ARDS, (2) fist measurements taken upon ICU admission, (3) patients with age >= 18. The exclusion criteria was patients with ICU stay duration less than 24 hours. The final data included 4,379 patients in total. These patients were combined into a single dataframe for further preprocessing, statistical analysis, and train-test split for modeling [4].



2.3. Feature Extraction

Based on our research and clinical expert suggestions, we organized our feature selection into several categories: demographics (Gender, Age, Height, Weight, Body Mass Index (BMI), Admission Type, Insurance, Race), vital signs (Heart Rate, Respiratory Rate, Temperature, Systolic Arterial Blood Pressure, Diastolic Arterial Blood Pressure, Mean Arterial Pressure (MAP), PaO2, PaCO2, SpO_2), laboratory values (Platelet Count, pH, Creatinine (mg/dL), Blood

Urea Nitrogen (BUN), Glucose, Sodium, White Blood Cell Count (WBC), Potassium, Albumin (g/L), Hematocrit (%), Hemoglobin, Hemoglobin (Hb), International Normalized Ratio (INR), Bicarbonate (mEq/L), C-Reactive Protein (CRP), Lactate, Bilirubin, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Absolute Neutrophil Count, Absolute Lymphocytes Count, Anion Gap), medical history/comorbidities (Diabetes, Peripheral Vascular Disease, Dementia, Peptic Ulcer Disease, Liver Disease, Paraplegia, Renal Disease, Congestive Heart Failure, Chronic Obstructive Pulmonary Disease, Pulmonary Disease (COPD), Heart Disease), severity scores (SAPS II, SOFA, APACHE II), and ICU/hospitalization related (Urine Output (Total Urine Output), Vasopressors, Inotropic Agents, Mechanical Ventilation, Intravenous Fluids (IV Fluids), Positive End-Expiratory Pressure (PEEP), Tidal Volume, Hemodialysis, ICU Length of Stay, Fraction of Inspired Oxygen (FiO2)) [5].

To ensure the accuracy and reliability of our modeling, all features were selected based on the first ICU admissions to eliminate the potential threat of any interventions happening after the ICU admissions. Some variables were selected differently based on the original dataset, for example, we used average values to extract vital signs [6]. And some variables were calculated based on other variables that are not included in the final dataset, for example, severity scores. In total, we have 60 features selected at the first stage. And we will make further investigations later for the feature selection part.

2.4. Data Preprocessing

The preprocessing process comprised several key steps. First, the dataset was divided into a training set (80%) and a testing set (20%) to prevent data leakage. Missing values for numerical variables were imputed using the median of each feature, while missing values for categorical variables were imputed using the mode (i.e., the most frequently occurring category).

To identify and handle outliers, the interquartile range (IQR) method was employed. Based on subsequent analysis, log transformation was applied to numerical variables exhibiting a significant number of outliers, in order to reduce skewness and preserve meaningful variation. For categorical variables, one-hot encoding was used to convert them into numerical format, facilitating compatibility with machine learning models. Finally, feature scaling was applied to numerical variables for models sensitive to differences in scale.

To retain all available patient records, row deletion was not considered during preprocessing. Additionally, recognizing that certain patients may present with extreme clinical values, log transformation was selectively used to accommodate such variability without loss of information. It is important to note that handling data imbalance was postponed until after feature selection.

This approach minimizes the introduction of noise into the synthetic data generated by SMOTE and enhances the quality and reliability of the feature selection process.

2.5 Feature Selection

The feature selection process carries out multiple stages to ensure that only the most statistically significant predictors were included for the final modeling process. The methodology included univariate analysis, multivariate modeling, and iterative backward elimination.

Initially, each independent variable was evaluated using a univariate logistic regression model. The objective was to assess the individual association of each variable with the binary outcome (in-hospital mortality). This was implemented using the *statsmodels* package, which allowed for the estimation of coefficients, standard errors, and p-values for each variable. Variables with a p-value less than 0.1 were considered to have a potentially significant impact with the outcome and were selected for further analysis. This relatively liberal threshold ($p < 0.1$) was chosen to avoid prematurely excluding variables that might become significant in a multivariable context when adjusted for confounding effects.

The subset of variables identified in the univariate step was used to construct a full multivariable logistic regression model [9]. This model included all selected predictors simultaneously, allowing for the examination of their independent contributions to the outcome while adjusting for the presence of other covariates.

Finally, to refine the model further and improve parsimony, a backward elimination procedure was performed based on Akaike information criterion (AIC). In this process, the variable with the highest p-value greater than 0.05 was removed from the model at each step. After each removal, the model was re-estimated using the remaining variables, and the process was repeated until all variables in the model had p-values less than or equal to 0.05. This step ensured that only statistically significant predictors (at the 5% level) remained in the final model.

Upon completion of the backward elimination process, the final model and the corresponding set of selected features were extracted. In total, we selected 21 features out of 60 features for our modeling process. Additionally, to ensure consistency between the training and testing phases, the test dataset was filtered to retain only the features selected in the final model. The constant (intercept) term was excluded from this filtering step. This ensured that the model could be accurately applied to the test data without introducing discrepancies in the feature space.

2.6. Modeling

To predict in-hospital mortality in sepsis-ARDS patients, we implemented several machine learning models: Random Forest, XGBoost, LightGBM, Support Vector Machine (SVM), Logistic Regression, and K-Nearest Neighbors (KNN). These models were selected for their ability to manage large datasets and handle complex, non-linear relationships that are common in clinical data.

Random Forest and XGBoost were chosen for their ensemble learning approach, which combines multiple decision trees to improve model accuracy and robustness. These models are particularly effective in handling high-dimensional feature spaces and avoiding overfitting, making them suitable for clinical prediction tasks. LightGBM, another gradient boosting method, was included due to its superior computational efficiency, especially with large datasets, and its capacity to deal with sparse data and categorical features [8].

SVM was selected because of its ability to find non-linear decision boundaries, which is particularly useful for complex datasets where linear separability is not always apparent. Logistic Regression was used as a baseline model, known for its simplicity, interpretability, and wide usage in medical settings. Finally, KNN, a non-parametric algorithm, was included for its simplicity and ability to model non-linear decision boundaries.

Hyperparameter tuning was conducted for each model to ensure optimal performance. Random Forest parameters such as the number of trees (n_estimators), maximum depth (max_depth), and the minimum number of samples required to split a node (min_samples_split) were optimized using GridSearchCV. For XGBoost and LightGBM, hyperparameters like the number of estimators (n_estimators), maximum depth (max_depth), and learning rate (learning_rate) were fine-tuned. SVM was optimized using Optuna, which selected the best penalty parameter (C) and kernel type. Logistic Regression had its regularization strength (C) adjusted, and for KNN, the optimal number of neighbors (n_neighbors), distance metric (metric), and weighting scheme (weights) were identified.

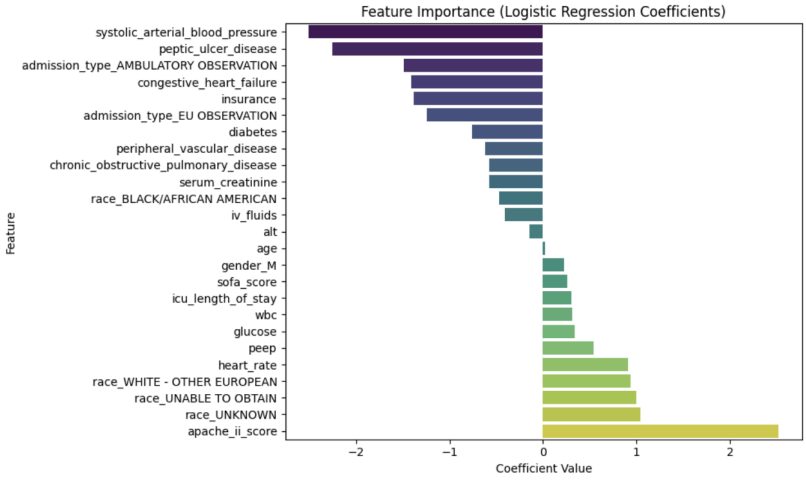
The performance of each model was evaluated using key metrics such as ROC-AUC, accuracy, sensitivity, and specificity. ROC-AUC was the primary evaluation metric as it provides a comprehensive measure of the model's ability to discriminate between the positive and negative classes across all possible classification thresholds. Accuracy was used to assess the overall proportion of correct classifications, while sensitivity measured the model's ability to correctly identify true positive cases, and specificity evaluated its ability to identify true negatives. These metrics provided a robust assessment of each model's effectiveness in predicting in-hospital mortality for sepsis-ARDS patients.

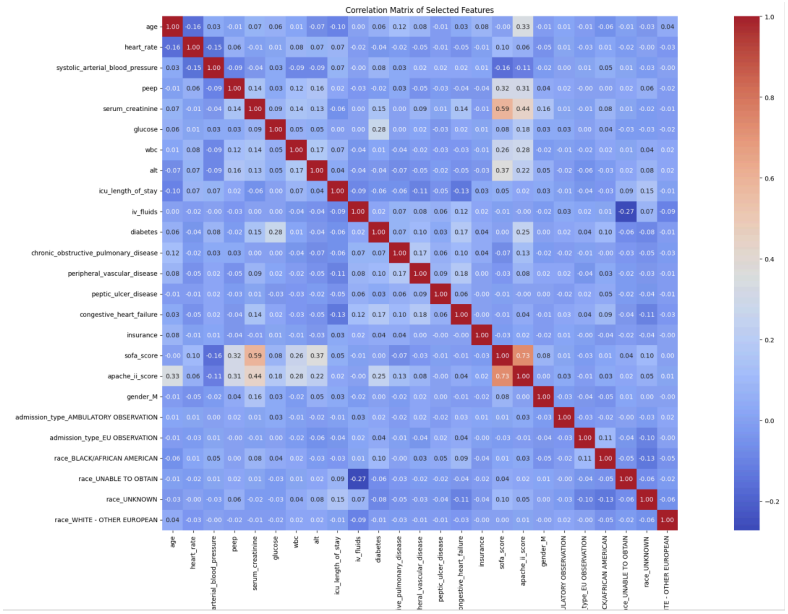
2.7. Statistical Analysis

Continuous variables with a normal distribution were summarized using the mean ± standard deviation, while those not following a normal distribution were reported as medians. The normality of continuous variables was evaluated using the Kolmogorov–Smirnov test. For group comparisons, normally distributed continuous variables were analyzed using the Student's t-test, whereas non-normally distributed data were compared using the Kruskal–Wallis H test [4]. Categorical variables were presented as frequencies or percentages and analyzed using the chi-square test or Fisher's exact test, depending on the sample size.

2.8. Feature Importance & Collinearity Elimination

To assess the contribution of individual predictors and ensure the interpretability of our final logistic regression model, we analyzed feature importance using model coefficients and evaluated inter-variable collinearity through a correlation matrix (graphs shown below). The feature importance plot reveals that clinical indicators such as systolic arterial blood pressure, peptic ulcer disease, and congestive heart failure had strong negative associations with in-hospital mortality, indicating protective effects. Conversely, severity scores like APACHE II, race-related variables, and physiological measurements like heart rate and PEEP demonstrated positive coefficients, highlighting their association with increased mortality risk. In parallel, the correlation matrix helped identify and mitigate multicollinearity issues. For instance, while SOFA and APACHE II scores showed moderate correlation ($r = 0.39$), most other features exhibited weak correlations ($r < 0.3$), supporting their independent contribution to the model. This dual assessment ensured that the final model retained statistically significant, non-redundant features, thereby enhancing model reliability and clinical interpretability.





3. RESULTS

3.1. Baseline & Multivariate Parameters Comparisons from Statistical Analysis

After our preprocessing and feature selection process, our final dataset contains 4,379 patients with 21 features, randomly splitted into training (80%) and testing (20%) sets. To further investigate the association between baseline clinical parameters and patient outcomes among individuals with sepsis and ARDS, several key indicators were identified as statistically significant ($p < 0.5$), suggesting their potential role in influencing patient prognosis.

The table below shows all the statistical outcomes for our analysis. Among the vital signs, heart rate (coef = 0.8458, p = 0.007), and PEEP (positive end-expiratory pressure) (coef = 0.5199, p = 0.001) were positively associated with the target variable (in-hospital mortality). Conversely, systolic arterial blood pressure was significantly and negatively associated (coef = -2.53, p < 0.001), indicating a protective effect. Laboratory values such as serum creatinine (coef = -0.4711, $p = 0.039$) and glucose (coef = 0.3463, $p = 0.017$) also demonstrated significant associations, as

did white blood cell count (WBC) (coef = 0.3033, $p = 0.001$), suggesting an inflammatory response relationship.

Several clinical comorbidities were predictive of poorer outcomes. Notably, diabetes (coef = -0.7267, $p < 0.001$), peptic ulcer disease (coef = -2.2918, $p = 0.013$), peripheral vascular disease (coef = -0.5970, $p = 0.016$), and congestive heart failure (coef = -1.3018, $p < 0.001$) were all significantly associated with worse prognosis. Clinical intervention-related variables, such as the use of intravenous fluids ($p = 0.005$) and ICU length of stay ($p < 0.001$), were also statistically significant. Regarding severity scores, both SOFA (coef = 0.2241, $p < 0.001$) and APACHE II (coef = 2.5369, $p < 0.001$) scores were strong predictors of outcomes, consistent with their clinical use in severity stratification. Significant disparities were also observed in some demographic and admission-related variables, including certain admission types and racial categories, highlighting potential social and systemic factors.

Overall, this multivariate logistic regression underscores the complex interaction between physiological, clinical, and demographic variables in influencing outcomes among patients with sepsis and ARDS, highlighting the necessity for individualized patient evaluation. The thorough statistical analysis conducted further affirmed the validity of the data partitioning strategy and reinforced the generalizability of the model's findings.

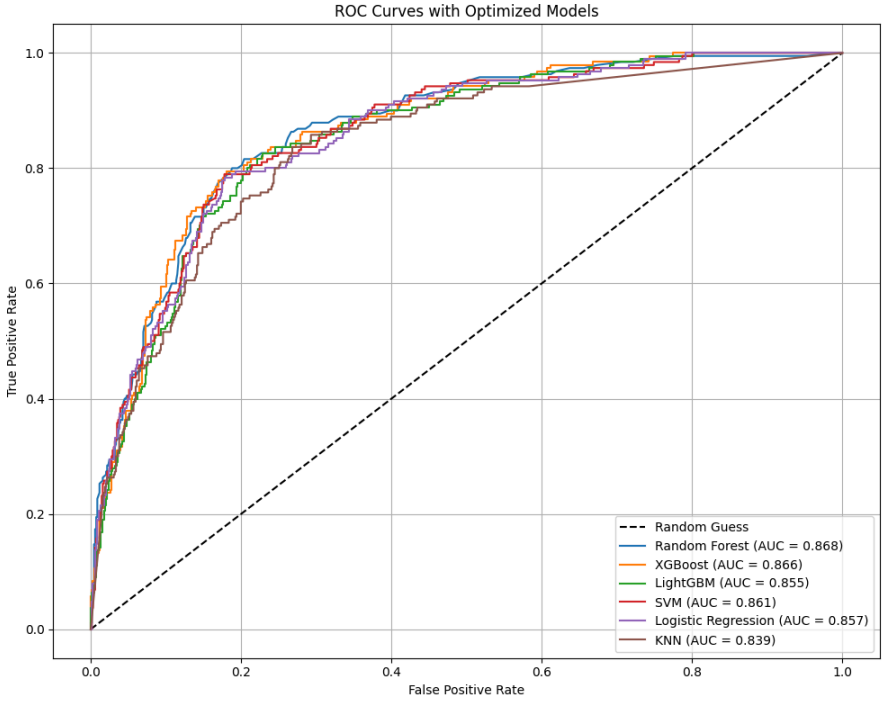
Feature Name	Coefficients	Standard Error	Z	P-Value
Heart Rate	0.8458	0.315	2.689	0.007
Systolic blood pressure	-2.53	0.574	-4.409	0
Age	0.0234	0.006	3.704	0
Race (White)	0.0916	0.174	0.526	0.599
Diabetes	-0.7267	0.135	-5.399	0
Peripheral Vascular	-0.597	0.249	-2.399	0.016
Peptic Ulcer	-2.2918	0.924	-2.48	0.013
Congestive Heart Failure	-1.3018	0.333	-3.906	0
SOFA	0.2241	0.062	3.616	0
APACHE II	2.5369	0.414	6.128	0
Admission Type (Urgent)	0.1178	0.141	0.836	0.403
ICU Length of Stay	0.297	0.071	4.205	0
Insurance	-1.3989	0.549	-2.55	0.011
IV Fluids	-0.6036	0.216	-2.796	0.005
Positive end-expiratory pressure (a respiratory setting, PEEP)	0.5199	0.152	3.412	0.001
Serum Creatinine	-0.4711	0.228	-2.062	0.039
Glucose	0.3463	0.145	2.384	0.017
White blood cell count, indicates infection or inflammation (WBC)	0.3033	0.089	3.407	0.001
Alanine aminotransferase , another liver enzyme indicating liver damage (ALT)	-0.1561	0.088	-1.773	0.076

3.2. Model Assessment

To evaluate the predictive performance of different machine learning algorithms for in-hospital mortality in sepsis patients with ARDS, we compared six models: Random Forest, XGBoost, LightGBM, Support Vector Machine (SVM), Logistic Regression, and K-Nearest Neighbors (KNN). Among these, Random Forest demonstrated the strongest overall performance with an accuracy of 82.88%, a specificity of 89.21%, and the highest ROC-AUC score of 0.8682, indicating a strong ability to distinguish between outcomes. XGBoost achieved slightly higher accuracy (83.56%) and specificity (89.94%), but with a marginally lower AUC (0.8660). Although SVM and Logistic Regression had slightly lower AUCs (0.8608 and 0.8574 respectively), they exhibited the highest sensitivity (0.7474 and 0.7368), making them potentially useful when prioritizing true positive identification. KNN performed the weakest across most

metrics, including the lowest AUC (0.8387). The ROC curve visualization confirmed these results, with the Random Forest model showing the best balance between sensitivity and specificity. Considering both performance and interpretability, Random Forest was selected as the final model due to its robustness and clinical relevance.

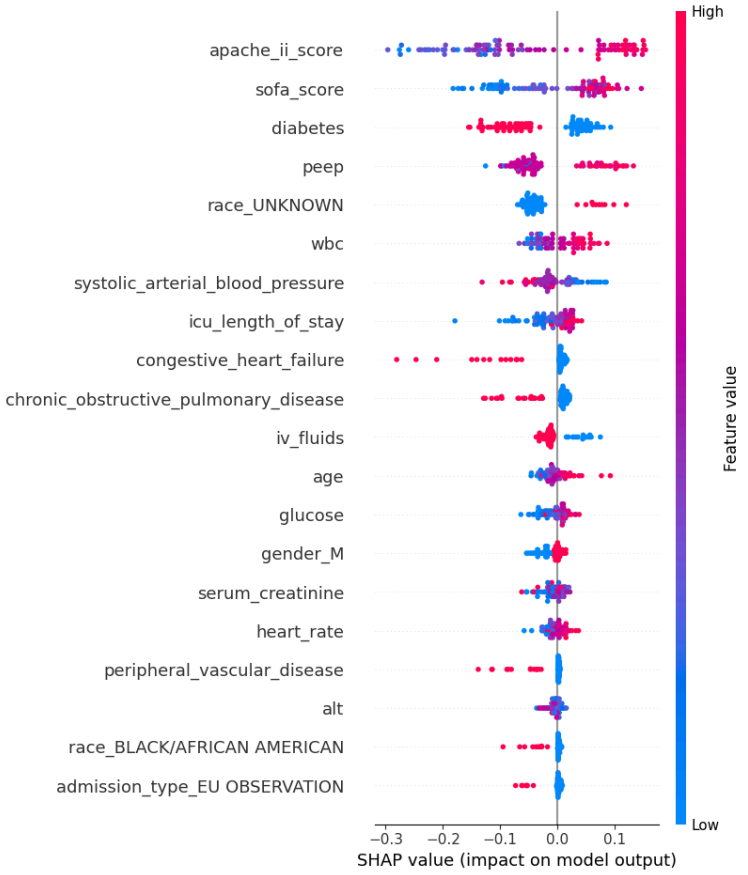
	Accuracy	Sensitivity	Specificity	ROC-AUC	95% CI Lower	95% CI Upper
Random Forest	**0.8288**	**0.6000**	**0.8921**	**0.8682**	**0.8389**	**0.8963**
XGBoost	0.8356	0.6053	0.8994	0.8660	0.8378	0.8946
LightGBM	0.8151	0.5684	0.8834	0.8549	0.8254	0.8839
SVM	0.8151	0.7474	0.8338	0.8608	0.8308	0.8894
Logistic Regression	0.8139	0.7368	0.8353	0.8574	0.8271	0.8862
KNN	0.8014	0.7000	0.8294	0.8387	0.8062	0.8706



3.3. SHAP Evaluation

To further interpret the contributions of individual features, SHAP (SHapley Additive exPlanations) analysis was conducted on the Random Forest model. The SHAP values provided insights into the significance of each feature in driving the model's predictions. Vital signs such as systolic arterial blood pressure, PEEP, and heart rate emerged as the most influential predictors, with PEEP showing a positive association with mortality, while systolic arterial blood

pressure exhibited a negative association, indicating its protective effect. Laboratory variables, including creatinine and glucose, were identified as critical determinants of patient outcomes, reinforcing the importance of metabolic and renal health in critically ill patients. This analysis underscores the interpretability of the model and facilitates clinical decision-making by quantifying the contribution of each variable to the predicted risk.



3.4. Study on Significant Variables for Selected Model

For the final model selection, Random Forest was chosen due to its high performance, particularly in terms of the ROC-AUC, accuracy, and specificity. Following model selection, we conducted a detailed analysis to identify the most significant features influencing the model's predictions of in-hospital mortality among sepsis-ARDS patients. This analysis was based on the variable importance derived from the Random Forest model, as well as insights gained from SHAP values, which provided a deeper understanding of how each feature contributed to the model's predictions.

The Random Forest model assigned varying levels of importance to different features. Among the most influential variables, systolic arterial blood pressure stood out, with a negative association with in-hospital mortality. This suggests that lower systolic arterial blood pressure is a strong indicator of poor outcomes, aligning with clinical knowledge that hypotension is a significant risk factor in sepsis and ARDS. Similarly, PEEP (positive end-expiratory pressure), a critical ventilatory parameter, was positively associated with mortality, indicating that higher PEEP levels may correlate with worse outcomes in patients with sepsis-induced ARDS.

Additional features of importance included heart rate, which was also positively associated with mortality risk, highlighting the role of tachycardia in deteriorating patient conditions. Creatinine and glucose levels were significant as well, reinforcing the role of renal function and metabolic control in patient outcomes. Glucose in particular, with higher levels correlating with worse prognosis, underscores the relevance of glucose management in critically ill patients.

From a clinical standpoint, severity scores such as SOFA and APACHE II emerged as strong predictors of mortality. These scores, which are commonly used in critical care settings to assess the severity of organ dysfunction and predict patient outcomes, were confirmed by the model as critical components in mortality prediction. Specifically, APACHE II had a particularly strong positive association with in-hospital mortality, consistent with its widespread use in ICU risk stratification.

Moreover, several comorbidities were identified as significant predictors. Diabetes, congestive heart failure, and renal disease were found to increase the risk of mortality, highlighting the importance of these chronic conditions in the prognosis of sepsis-ARDS patients. These findings align with the literature that indicates comorbid conditions often exacerbate the course of sepsis and ARDS, making early intervention crucial for these patients.

The SHAP analysis provided a more granular understanding of the impact of each feature on the model's predictions. It revealed that variables such as systolic arterial blood pressure and PEEP not only had high feature importance but also had large SHAP values, indicating that they were not only important but also highly influential in the model's decision-making process. This analysis enhanced the interpretability of the model, offering valuable insights into which clinical factors should be prioritized when assessing patient risk for in-hospital mortality.

In conclusion, the study of significant variables for the Random Forest model highlighted the critical role of physiological parameters such as systolic arterial blood pressure, PEEP, and heart rate, along with laboratory values like creatinine and glucose. Additionally, severity scores and comorbidities were pivotal in understanding the patient’s risk profile, providing actionable insights for improving early mortality risk stratification in sepsis-ARDS patients.

4. DISCUSSION

4.1. General Improvement Summary

Our research achieved improved model performance through several key enhancements in data handling, feature engineering, and model optimization. We collected data from updated and reliable open-source platforms, ensuring relevance and reducing the influence of extreme or volatile external factors. A more comprehensive yet carefully curated set of features was selected, with adjustments made to enhance predictive power while eliminating incomplete or potentially misleading variables. We also introduced novel features that added value to the modeling process. Additionally, we employed advanced hyperparameter tuning techniques—such as Grid Search and Bayesian Optimization—tailored to each model, allowing for more precise optimization and stronger overall performance. These methodological improvements collectively led to more accurate, stable, and generalizable predictive outcomes.

4.2. Limitations and Future Work

While our predictive models demonstrated strong performance, several limitations should be acknowledged. First, although we used updated open-source data from the MIMIC-IV database, the model was trained and validated on a single-center dataset, which may limit its generalizability to broader populations. Additionally, although our feature selection process was refined compared to prior studies, it is possible that other relevant predictors were not included, and further validation with external variables is needed. Hyperparameter tuning was carefully applied to each model, enhancing performance, but this also increases complexity in replication. Looking ahead, we aim to apply our models in real-world clinical settings to evaluate their practical utility. We also plan to incorporate additional open-source datasets to validate model robustness across institutions and expand the feature set to further improve predictive power.

5. CONCLUSION

In this study, we developed and validated a clinical prediction model for in-hospital mortality among patients with sepsis complicated by Acute Respiratory Distress Syndrome (ARDS), using data from the MIMIC-IV database. By incorporating a comprehensive set of clinical

features—including demographic information, vital signs, laboratory values, comorbidities, and severity scores—we identified 21 significant predictors through rigorous statistical and machine learning techniques [10]. The model demonstrated strong predictive performance and provided meaningful insights into the clinical factors most associated with poor outcomes in this high-risk population. Additionally, the application of SHAP analysis offered interpretability by quantifying each variable's contribution to the model's predictions. Our findings underscore the importance of early identification of high-risk patients and support the potential for data-driven tools to enhance clinical decision-making in critical care settings. Future work should focus on external validation in diverse cohorts, integration with real-time ICU systems, and prospective evaluation of the model’s impact on clinical workflows and patient outcomes.

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